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- 1. A nucleic acid encoding a polypeptide of between 150 and 299 amino acids that has an amino acid sequence at least 50% identical to that of the corresponding region of amino acids 1 to 299 of a mature, native human apoE polypeptide and that, when administered to or expressed in a mammal, lowers the total serum cholesterol level without inducing hypertriglyceridemia.
- 2. The nucleic acid of claim 1, encoding a polypeptide that has an amino acid sequence at least 80% identical to the corresponding region of a mature, native human apoE.
- 3. The nucleic acid of claim 2, encoding a polypeptide that has an amino acid sequence 100% identical to the corresponding region of a mature, native, human apoE.
- 4. The nucleic acid of claim 1, wherein the amino acid sequence of said encoded polypeptide is at least 80% identical to the corresponding region of a mature, native human apoE polypeptide, beginning at amino acid residue 1.
- 5. The nucleic acid of claim 1, wherein said encoded polypeptide has a signal peptide operably linked to said region of said mature apoE.
- 6. The nucleic acid of claim 1, wherein said encoded polypeptide consists of between 150 and 215 amino acids.
- 7. The hucleic acid of claim 1, wherein said encoded polypeptide consists of 203 amino acids.

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- 8. The nucleic acid of claim 1, encoding residues 1-203 of an apoE preprotein of any one of SEQ ID Nos. 14-19.
- 9. The nucleic acid of claim 1, wherein said encoded polypeptide consists of 220 amino acids.
- 5 10. The nucleic acid of claim 1, encoding residues 1-220 of an apoE preprotein of any one of SEQ ID Nos. 14-19.
  - 11. The nucleic acid of claim 1, wherein said encoded polypeptide consists of 247 amino acids.
  - 12. The nucleic acid of claim 1, encoding residues 1-247 of an apoE preprotein of any one of SEQ ID Nos. 1/4-19.
  - 13. The nucleic acid of claim 1, wherein said encoded polypeptide consists of 277 amino acids.
  - 14. The nucleic acid of claim 1, encoding residues 1-277 of an apoE preprotein of any one of SEQ ID Nos. 14-19.
  - 15. A polypeptide of between 150 and 299 amino acids, said polypeptide having an amino acid sequence at least 50% identical to the corresponding region of amino acids 1-299 of a mature, native, human apoE, said polypeptide, when administered to or expressed in a mammal, being capable of lowering the total serum cholesterol level without inducing hypertriglyceridemia.

- 16. The polypeptide of claim 15, having an amino acid sequence at least 80% identical to the corresponding region of a mature, native, human apoE.
- 17. The polypeptide of claim 16, having an amino acid sequence 100% identical to the corresponding region of a mature, native, human apoE.
  - 18. The polypeptide of claim 15, having an amino acid sequence at least 80% identical to the corresponding region of a mature, native, human apoE polypeptide, beginning at amino acid residue 1.
- 19. The polypeptide of claim 15, consisting of between 150 and 215 amino acids.
  - 20. The polypepide of claim 15, having an amino acid sequence identical to amino acids 1-185 of a mature, native human apoE of any one of SEQ ID Nos. 1-6.
  - 21. The polypepide of claim 15, having an amino acid sequence identical to amino acids 1-202 of a mature, native human apoE of any one of SEQ ID Nos. 1-6.
  - 22. The polypepide of claim 15, having an amino acid sequence identical to amino acids 1-229 of a mature, native human apoE of any one of SEQ ID Nos. 1-6.
  - 23. The polypepide of claim 15, having an amino acid sequence identical to amino acids 1-259 of a mature, native human apoE of any one of SEQ ID Nos. 1-6.

- 24. A method of lowering cholesterol, delaying the onset of atherosclerosis, or treating atherosclerosis in a mammal without inducing hypertriglyceridemia, said method comprising administering to said mammal a polypeptide of between 150 and 299 amino acids, said polypeptide having an amino acid sequence at least 80% identical to the corresponding region of amino acids 1-299 of a mature, native, human apoE, said polypeptide, when administered to or expressed in a mammal, being capable of lowering the total serum cholesterol level without inducing hypertriglyceridemia.
- 25. The method of claim 24, wherein said mammal lacks an endogenous, normally functioning apoE gene.
  - 26. The method of claim 24, wherein said mammal is at risk for developing atherosclerosis due to accumulation of lipoprotein remnants in the bloodstream.
  - 27. The method of claim 26, wherein said mammal has a defect in remnant removal.
  - 28. The method of claim 24, wherein said mammal lacks an endogenous, normally functioning LDL receptor.
  - 29. The method of claim 24, wherein said polypeptide is administered intramuscularly, intravenously, or subcutaneously to said mammal.
- 30. A method of lowering cholesterol, delaying the onset of
  atherosclerosis, or regressing atherosclerosis in a mammal without inducing hypertriglyceridemia, said method comprising administering to or expressing in said mammal a nucleic acid encoding a polypeptide of between 150 and 299

amino acids that has an amino acid sequence at least 80% identical to that of the corresponding region of amino acids 1 to 299 of a mature, native, human apoE polypeptide and that, when administered to or expressed in a mammal, lowers the total serum cholesterol level without inducing hypertriglyceridemia.

- 5 31. The method of claim 30, wherein said nucleic acid is operably linked to a promoter and contained in an expression vector.
  - 32. The method of claim 30, wherein said nucleic acid is intravenously administered to said mammal in combination with a liposome and protamine.
  - 33. The method of claim 30, wherein said nucleic acid is contained in a recombinant viral vector.
  - 34. The method of claim 33, wherein said vector is administered intravenously.
  - 35. The method of claim 33, wherein said vector is administered by bone marrow transplantation.
- 36. The method of claim 33, wherein said vector is administered to an artery at the site of a lesion.
  - 37. The method of claim 33, wherein said vector is an adenoviral vector.
  - 38. The method of claim 33, wherein said vector is an adeno-associated viral vector.

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- 39. The method of claim 33, wherein said vector is a lentiviral vector.
- 40. The method of claim 33, wherein said vector is a herpes viral vector.
- 41. The method of claim 33, wherein said vector is a retroviral vector.
- 42. The method of claim 33, wherein said vector is a baculoviral vector.
- 43. The method of claim 30, wherein said mammal lacks an endogenous, normally functioning apoE gene.
- 44. The method of claim 30, wherein said mammal is at risk for developing atherosclerosis due to accumulation of lipoprotein remnants in the bloodstream.
- 45. The method of claim 40, wherein said mammal has a defect in remnant removal.
- 46. The method of claim 30, wherein said mammal lacks an endogenous, normally functioning LDL receptor.
- 47. The method claim of 30, wherein said nucleic acid is administered to or expressed in the liver of said mammal.
- 48. A pharmaceutical composition comprising a polypeptide admixed with a pharmaceutically acceptable carrier substance, said polypeptide consisting of between 150 and 299 amino acids and having an amino acid sequence at least 80% identical to the corresponding region of amino acids 1-299 of a mature, native, human apoE, said polypeptide, when administered to or expressed in a mammal,

being capable of lowering the total serum cholesterol level without inducing hypertriglyceridemia.

49. A recombinant DNA molecule comprising a nucleic acid operatively linked to a promoter, said nucleic acid encoding a polypeptide of between 150 and 299 amino acids that has an amino acid sequence at least 80% identical to that of the corresponding region of amino acids 1 to 299 of a mature, native, human apoE polypeptide and that, when administered to or expressed in a mammal, lowers the total serum cholesterol level without inducing hypertriglyceridemia.

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